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1: P00379. Dihydrofolate reductase [gi:118974]

LOCUS P00379 159 aa linear BCT 15-MAR-2004

DEFINITION Dihydrofolate reductase.

ACCESSION P00379

VERSION P00379 GI:118974

DBSOURCE swissprot: locus DYC_ECOLI, accession P00379; class: standard.

created: Jul 21, 1986.

sequence updated: Jul 21, 1986.

annotation updated: Mar 15, 2004.

xrefs: gi: [146005](#), gi: [146006](#), gi: [41264](#), gi: [41265](#), gi: [21321891](#), gi: [21321929](#), gi: [1786230](#), gi: [1786233](#), gi: [26106314](#), gi: [26106368](#), gi: [24050246](#), gi: [24050247](#), gi: [30039813](#), gi: [30039857](#), gi: [66098](#), pdb accession 4DFR, gi: [231129](#), gi: [231205](#), gi: [231252](#), pdb accession 1DRA, pdb accession 1DRB, pdb accession 2DRC, pdb accession 3DRC, pdb accession 1DHI, pdb accession 1DHJ, pdb accession 1DDR, pdb accession 1DDS, gi: [1942148](#), gi: [996100](#), pdb accession 1DYH, pdb accession 1DYI, pdb accession 1DYJ, pdb accession 1JOL, gi: [1943514](#), gi: [1942814](#), gi: [1942742](#), gi: [1942743](#), gi: [1941993](#), gi: [1942744](#), pdb accession 1RB2, pdb accession 1RB3, gi: [1942006](#), pdb accession 1RD7, pdb accession 1RE7, gi: [1942023](#), gi: [1942024](#), gi: [1942025](#), gi: [1942605](#), gi: [1942541](#), gi: [1942542](#), gi: [1942543](#), gi: [1942544](#), gi: [1942545](#), gi: [1942030](#), gi: [1942031](#), gi: [2098461](#), pdb accession 1TDR

xrefs (non-sequence databases): SWISS-2DPAGEP00379, ECO2DBASEB020.0, EcoGeneEG10326, InterProIPR001796, PfamPF00186, PRINTSPR00070, PROSITEPS00075

KEYWORDS Oxidoreductase; NADP; Trimethoprim resistance; Methotrexate resistance; One-carbon metabolism; 3D-structure; Complete proteome.

SOURCE Escherichia coli

ORGANISM Escherichia coli

Bacteria; Proteobacteria; Gammaproteobacteria; Enterobacteriales; Enterobacteriaceae; Escherichia.

REFERENCE 1 (residues 1 to 159)

AUTHORS Smith, D.R. and Calvo, J.M.

TITLE Nucleotide sequence of the E. coli gene coding for dihydrofolate reductase

JOURNAL Nucleic Acids Res. 8 (10), 2255-2274 (1980)

MEDLINE [81053692](#)

PUBMED [6159575](#)

REMARK SEQUENCE FROM N.A.

SPECIES=E. coli; STRAIN=K12

REFERENCE 2 (residues 1 to 159)

AUTHORS Yura, T., Mori, H., Nagai, H., Nagata, T., Ishihama, A., Fujita, N., Isono, K., Mizobuchi, K. and Nakata, A.

TITLE Systematic sequencing of the Escherichia coli genome: analysis of the 0-2.4 min region

JOURNAL Nucleic Acids Res. 20 (13), 3305-3308 (1992)

MEDLINE [92334977](#)

PUBMED [1630901](#)

REMARK SEQUENCE FROM N.A.
SPECIES=E.coli; STRAIN=K12

REFERENCE 3 (residues 1 to 159)

AUTHORS Blattner,F.R., Plunkett,G. III, Bloch,C.A., Perna,N.T., Burland,V., Riley,M., Collado-Vides,J., Glasner,J.D., Rode,C.K., Mayhew,G.F., Gregor,J., Davis,N.W., Kirkpatrick,H.A., Goeden,M.A., Rose,D.J., Mau,B. and Shao,Y.

TITLE The complete genome sequence of *Escherichia coli* K-12

JOURNAL Science 277 (5331), 1453-1474 (1997)

MEDLINE 97426617

PUBMED 9278503

REMARK SEQUENCE FROM N.A.
SPECIES=E.coli; STRAIN=K12 / MG1655

REFERENCE 4 (residues 1 to 159)

AUTHORS Welch,R.A., Burland,V., Plunkett,G. III, Redford,P., Roesch,P., Rasko,D., Buckles,E.L., Liou,S.-R., Boutin,A., Hackett,J., Stroud,D., Mayhew,G.F., Rose,D.J., Zhou,S., Schwartz,D.C., Perna,N.T., Mobley,H.L.T., Donnenberg,M.S. and Blattner,F.R.

TITLE Extensive mosaic structure revealed by the complete genome sequence of uropathogenic *Escherichia coli*

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (26), 17020-17024 (2002)

MEDLINE 22388234

PUBMED 12471157

REMARK SEQUENCE FROM N.A.
SPECIES=E.coli; STRAIN=O6:H1 / CFT073 / ATCC 700928

REFERENCE 5 (residues 1 to 159)

AUTHORS Stone,D., Phillips,A.W. and Burchall,J.J.

TITLE The amino-acid sequence of the dihydrofolate reductase of a trimethoprim-resistant strain of *Escherichia coli*

JOURNAL Eur. J. Biochem. 72 (3), 613-624 (1977)

MEDLINE 77115802

PUBMED 320005

REMARK SEQUENCE (ISOZYME 1).
SPECIES=E.coli; STRAIN=B [RT500]

REFERENCE 6 (residues 1 to 159)

AUTHORS Baccanari,D.P., Stone,D. and Kuyper,L.

TITLE Effect of a single amino acid substitution on *Escherichia coli* dihydrofolate reductase catalysis and ligand binding

JOURNAL J. Biol. Chem. 256 (4), 1738-1747 (1981)

MEDLINE 81117257

PUBMED 7007370

REMARK SEQUENCE (ISOZYME 2).
SPECIES=E.coli; STRAIN=B [RT500]

REFERENCE 7 (residues 1 to 159)

AUTHORS Bennett,C.D., Rodkey,J.A., Sondey,J.M. and Hirschmann,R.

TITLE Dihydrofolate reductase: the amino acid sequence of the enzyme from a methotrexate-resistant mutant of *Escherichia coli*

JOURNAL Biochemistry 17 (7), 1328-1337 (1978)

MEDLINE 78187252

PUBMED 350268

REMARK SEQUENCE.
SPECIES=E.coli; STRAIN=B [MB1428]

REFERENCE 8 (residues 1 to 159)

AUTHORS Flensburg,J. and Skold,O.

TITLE Massive overproduction of dihydrofolate reductase in bacteria as a response to the use of trimethoprim

JOURNAL Eur. J. Biochem. 162 (3), 473-476 (1987)

MEDLINE 87161813

PUBMED 3549289

REMARK SEQUENCE FROM N.A.

SPECIES=E.coli; STRAIN=1810
REFERENCE 9 (residues 1 to 159)
AUTHORS Jin,Q., Yuan,Z., Xu,J., Wang,Y., Shen,Y., Lu,W., Wang,J., Liu,H., Yang,J., Yang,F., Zhang,X., Zhang,J., Yang,G., Wu,H., Qu,D., Dong,J., Sun,L., Xue,Y., Zhao,A., Gao,Y., Zhu,J., Kan,B., Ding,K., Chen,S., Cheng,H., Yao,Z., He,B., Chen,R., Ma,D., Qiang,B., Wen,Y., Hou,Y. and Yu,J.
TITLE Genome sequence of *Shigella flexneri* 2a: insights into pathogenicity through comparison with genomes of *Escherichia coli* K12 and O157
JOURNAL Nucleic Acids Res. 30 (20), 4432-4441 (2002)
MEDLINE 22272406
PUBMED 12384590
REMARK SEQUENCE FROM N.A.
SPECIES=S.flexneri; STRAIN=301 / Serotype 2a
REFERENCE 10 (residues 1 to 159)
AUTHORS Wei,J., Goldberg,M.B., Burland,V., Venkatesan,M.M., Deng,W., Fournier,G., Mayhew,G.F., Plunkett,G. III, Rose,D.J., Darling,A., Mau,B., Perna,N.T., Payne,S.M., Runyen-Janecky,L.J., Zhou,S., Schwartz,D.C. and Blattner,F.R.
TITLE Complete genome sequence and comparative genomics of *Shigella flexneri* serotype 2a strain 2457T
JOURNAL Infect. Immun. 71 (5), 2775-2786 (2003)
MEDLINE 22590274
PUBMED 12704152
REMARK SEQUENCE FROM N.A.
SPECIES=S.flexneri; STRAIN=2457T / ATCC 700930 / Serotype 2a
REFERENCE 11 (residues 1 to 159)
AUTHORS Filman,D.J., Bolin,J.T., Matthews,D.A. and Kraut,J.
TITLE Crystal structures of *Escherichia coli* and *Lactobacillus casei* dihydrofolate reductase refined at 1.7 Å resolution. II. Environment of bound NADPH and implications for catalysis
JOURNAL J. Biol. Chem. 257 (22), 13663-13672 (1982)
MEDLINE 83056868
PUBMED 6815179
REMARK X-RAY CRYSTALLOGRAPHY (1.7 ANGSTROMS).
SPECIES=E.coli
REFERENCE 12 (residues 1 to 159)
AUTHORS Bystroff,C., Oatley,S.J. and Kraut,J.
TITLE Crystal structures of *Escherichia coli* dihydrofolate reductase: the NADP⁺ holoenzyme and the folate-NADP⁺ ternary complex. Substrate binding and a model for the transition state
JOURNAL Biochemistry 29 (13), 3263-3277 (1990)
MEDLINE 90241903
PUBMED 2185835
REMARK X-RAY CRYSTALLOGRAPHY.
SPECIES=E.coli
REFERENCE 13 (residues 1 to 159)
AUTHORS Bystroff,C. and Kraut,J.
TITLE Crystal structure of unliganded *Escherichia coli* dihydrofolate reductase. Ligand-induced conformational changes and cooperativity in binding
JOURNAL Biochemistry 30 (8), 2227-2239 (1991)
MEDLINE 91152037
PUBMED 1998681
REMARK X-RAY CRYSTALLOGRAPHY (2.3 ANGSTROMS).
SPECIES=E.coli

COMMENT This SWISS-PROT entry is copyright. It is produced through a collaboration between the Swiss Institute of Bioinformatics and

the EMBL outstation - the European Bioinformatics Institute.
The original entry is available from <http://www.expasy.ch/sprot>
and <http://www.ebi.ac.uk/sprot>

[CATALYTIC ACTIVITY] 5,6,7,8-tetrahydrofolate + NADP(+) =
7,8-dihydrofolate + NADPH.
[PATHWAY] Essential step for de novo glycine and purine synthesis,
DNA precursor synthesis, and for the conversion of dUMP to dTMP.
[MISCELLANEOUS] The strain K12 sequence is shown.
[MISCELLANEOUS] STRAIN B [RT500] IS RESISTANT TO 500 MICROGRAMS PER
MILLILITER OF TRIMETHOPRIM.
[MISCELLANEOUS] STRAIN B [MB1428] IS METHOTREXATE-RESISTANT.
[SIMILARITY] Belongs to the dihydrofolate reductase family.

FEATURES	Location/Qualifiers
source	1..159 /organism="Shigella flexneri" /db_xref="taxon:623"
source	1..159 /organism="Escherichia coli O6" /db_xref="taxon:217992"
source	1..159 /organism="Escherichia coli" /db_xref="taxon:562"
gene	1..159 /gene="FOLA" /note="synonyms: TMRA, B0048, C0058, SF0045, S0047"
Protein	1..159 /gene="FOLA" /product="Dihydrofolate reductase" /EC_number="1.5.1.3"
Region	2..8 /gene="FOLA" /region_name="Beta-strand region"
Region	10..12 /gene="FOLA" /region_name="Helical region"
Region	13..15 /gene="FOLA" /region_name="Beta-strand region"
Region	25..35 /gene="FOLA" /region_name="Helical region"
Region	28 /gene="FOLA" /region_name="Variant" /note="L -> R (IN STRAIN B[RT500] ISOZYME 2)."
Region	30 /gene="FOLA" /region_name="Variant" /note="W -> G (IN STRAIN 1810)."
Region	36..37 /gene="FOLA" /region_name="Hydrogen bonded turn"
Region	40..43 /gene="FOLA" /region_name="Beta-strand region"
Region	44..50 /gene="FOLA" /region_name="Helical region"
Region	55..56

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Region      84..85
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Region      97..103
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Region      104..106
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Region      109..115
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        /region_name="Beta-strand region"
Region      123..124
        /gene="FOLA"
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Region      130..132
        /gene="FOLA"
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Region      133..141
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        /region_name="Beta-strand region"
Region      151..159
        /gene="FOLA"
        /region_name="Beta-strand region"
Region      154
        /gene="FOLA"
        /region_name="Variant"
        /note="E -> Q (IN STRAIN 1810)."
Region      154
        /gene="FOLA"
        /region_name="Variant"
        /note="E -> K (IN STRAIN B[MB1428])."
ORIGIN
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  121 gdthfpdyep ddwesvfsef hdadaqnshs ycfeilerr
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Jan 20 2004 07:47:23